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Outline For

OFFICE OF NAVAL RESEARCH

Microbiology Branch

SEMI-ANNUAL PROGRESS REPORT

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TITLE OF PROJECT: ACUTE RESPIRATORY INFECTIONS

Objectives: 1. Study of acute beta hemolytic streptococcic infections.

An attempt to relate antigenic and enzymatic properties of infecting strains to clinical and antibody responses of individual patients is still considered one of the prim objectives of the project. At present the investigation has narrowed down to a study particularly of the type - specific M substance of Lancefield and its antibody in convalescents in relation to antibiotic therapy. The problem of hyaluronidase production in vivo is also being studied now. This work depends in a large part on the supply of untreated patients with streptococcal infections - obviously a possible bottle-neck. Along with the subjects noted above, work on the mechanism of resistance to phagocytosis exhibited by these organisms will proceed with emphasis on the relation between hyaluronic acid and the M substance.

2. Study of acute respiratory diseases of unknown or obscure etiology, with emphasis on the search for etiologic agents hitherto unknown. The plan of attack was developed and maintained in accord with a conviction that the general approach to this difficult field must take advantage of promising developments. Correlation of knowledge available to the investigators is considered fundamental. Repetition of methods, or study of diseases already under appropriate scrutiny, are not intended. The recognition of common infections is necessary, but incidental, during the search for other entities. A search for methods and for concepts, other than those already explored by competent investigators, seems important. Application of new methods for isolation of infectious agents and of more effective serologic or other techniques is essential. At any time, circumstances may dictate a change in approach not now apparent. A solution to problems of prevention and control of acute respiratory infections of known or unknown etiology is the major ultimate objective of all aspects of these studies.

Abstract of Results:

1. In attempting to assess the factors responsible for virulence, it is felt that one of the most important factors is resistance to phagocytosis in the presence of serum devoid of specific immune bodies. It has been necessary to develop techniques which possess high degrees of specificity and reproducibility. The experiments to date indicate a possible interrelation between hypothetical capsular M substance and hyaluronic acid; however, these experiments have not been extensive enough to warrant a more definitive statement at this time. It is expected that continued investigation will yield definite results to be presented in the next semi-annual report.

   A few more sera collected from treated and untreated patients convalescent from beta hemolytic streptococcal infections have been examined for the presence of anti - M immune bodies. Lack of sufficient number of serum samples continues to prevent a statistically significant report of the results of the experiments.

2.a. Studies on the Role of Coxsackie Virus in Respiratory Disease

The first objective was to discover whether or not Coxsackie viruses are present in incoming recruits from various parts of the country.

In July, 1951, preliminary studies were begun and, at the time of the last report, stools from 72 healthy young recruits had been screened for the presence of Coxsackie virus. The survey has since been enlarged to a total of 200 stool specimens screened for Coxsackie virus by inoculation of suckling mice. No isolation of C virus were made from these 200 speciments although isolations were made from an ill laboratory worker at NAMRU-4 and from an ill child in Madison. Initially the inoculation of mice was carried out at the University of Wisconsin. During the latter part of the study, inoculations were done at NAMRU-4 using suckling mice provided by the University of Wisconsin.

b. The Use of Newly Developed Techniques for Attempts to Isolate Specific Etiologic Agents so Far Unknown

This work has been continued by Dr. Lois Kitze. Using specimens obtained from patients at the University of Wisconsin, isolation attempts have been made in tissue culture and in mice treated with cortisone. Those specimens so-far studied have largely been from patients believed to have infectious mononucleosis or mild, non-bacterial upper respiratory infections. This work is getting well under-way. No specific isolations have been accomplished to date.

c. Further Refinement of Diagnostic Techniques

To establish techniques for study of agents and sera pertinent to this project, the plate complement fixation method of Fulton and Dumbell was selected and standardized. A study is being carried out to compare the sensitivity and accuracy of this method with that of the standard tube method using influenza, mumps and coxsackie antigen-antibody systems.

d. Results of studies employing the electroencephalograph to detect the presence of central nervous system involvement during acute infections of various types have been sufficiently revealing to suggest further emphasis on continuation.

Plans For Future:

Immediate:

1. Research on streptococcal disease will probably be mainly devoted to the question of virulence or invasiveness. The problem is difficult and the direction of study almost impossible to anticipate. The possible interrelation of the M substance in hyaluronic acid has received attention. These investigations will continue.

2. Isolation experiments with specimens from patients with acute respiratory diseases will be continued to evaluate the significance, if any, of vesicular stomatitis, Newcastle disease, Herpes simplex, and influenza. Suitable groups of Naval recruits and University students with respiratory infections will have serologic studies continued for the purpose of survey for Q fever, lymphocytic choriomeningitis, Psittacosis-lymphogranuloma group, and mumps.

Long Range:

The long range objectives are essentially those outlined in the original proposal and previous Progress Reports. The principle of approach and objectives outlined therein and at the beginning of this Report have not been altered by the experience to date. Results so far have not suggested a major change.

A concentrated effort, utilizing the techniques available, to isolate an agent which may be etiologic for common acute respiratory infections of unknown cause is considered of most importance to the long range study. It is not likely that many specimens from any group of patients can receive the time consuming efforts required to effectively exhaust the methods. It is critical to the isolation experiments that those concerned employ the utmost judgment in the selection of suitable patients and of appropriate specimens. The discovery of one hitherto unknown agent would become a significant contribution and thus justify the efforts expended in a series of negative experiments.

The long range plans include further exploration of several animal diseases which are potentially pathogenic for man. Epidemiologists from Veterinary Science and from the Medical School will make surveys together to include humans and other animals at the same site as feasible.

Other long term aspects include evaluation of conditions such as infectious mononucleosis, infectious hepatitis, and leptospirosis.

REPORTS AND PUBLICATIONS:

Quinn, R. W., Seastone, C. V. and Weber, R. W.: The Relationship of the Antigenic Characteristics of Streptococci and Specific Antibody Responses Following Streptococcal Infections. J. Infectious Diseases. In Press.

(Two copies of this paper have been submitted in lieu of a Technical Report.)